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Perspective

Carbon-Footprint Analyses in RCTs — Toward Sustainable Clinical Practice

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Human-induced climate change and destruction of nature is a global health emergency. By 2030, an estimated 2 billion people will reside in areas considered to be not well suited for sustaining human life.[1] Extreme weather events, water and food insecurity, and the risk of infectious diseases are increasing. Immediate action to reduce greenhouse-gas emissions in all sectors of society is paramount to support a livable future.

Health care is a substantial contributor to the current environmental crisis. In 2021, the 26th United Nations Climate Change Conference health program urged the health care community to reduce emissions by building low-carbon, sustainable health care systems. But knowledge about the carbon footprints of existing health care interventions and how best to assess the environmental effects of new tests, treatments, and services in relation to their clinical benefits has been limited. As a result, it's been difficult to make evidence-based decisions focused on using clinically effective and climate-friendly interventions.

Evaluation of new interventions typically involves conducting randomized, controlled trials (RCTs) that assess clinical benefits and harms. Only after clinical implementation, if at all, have the environmental effects of some interventions typically been assessed. We believe that an intervention's carbon footprint should be examined in parallel with its clinical benefits and harms. Clinical trial infrastructure is designed to generate high-quality data and may be well suited for conducting carbon-footprint analyses of interventions with the same rigor and control in design and conduct as assessments of clinical end points. These data could inform decisions by regulators and policymakers, thereby supporting the use of interventions with the lowest possible environmental burden.

The preferred method for quantification of the carbon footprint and other environmental effects of health care interventions is life-cycle assessment (LCA). LCAs are systematic analyses that evaluate the environmental effects of products (or processes involving various products) from raw-materials extraction through production, use, and disposal or recycling. LCA takes into account a wide range of environmental effects. Among these effects, an intervention's carbon footprint reflects its global warming potential. This measure is expressed in carbon dioxide equivalents, which repre-

sent the total amount of carbon dioxide and other greenhouse gases emitted. Other categories of environmental effects include land and water use, acidification, biodiversity loss, and effects on human health. Given the immediate need for emissions reductions and to align with reporting standards in other sectors, we suggest that clinical trials include an environmental impact analysis with carbon footprint as an end point.

When estimating a medical intervention's carbon footprint, it's essential to include environmental effects occurring after the intervention is complete, which would be facilitated by the comprehensive follow-up that is conducted in most clinical trials.

We (the authors) recently started using carbon footprint as a secondary end point in RCTs and found that most of the data needed to estimate it are also relevant for patient outcomes and health economic analysis and are therefore already included in trial protocols. One of our ongoing trials is comparing surgical and endoscopic removal of early colon cancer (ClinicalTrials.gov number, NCT06057350). In addition to using main end points that reflect clinical benefits and harms, we will be performing an environmental impact analysis to assess the carbon footprints of the two interventions, including greenhouse-gas emissions related to postintervention follow-up, complications, and cancer recurrences.

Another trial is investigating surgery as compared with glucocorticoid injections in patients with carpal tunnel syndrome (Clinical Trials.gov number, NCT05306548). The carbon footprint of the injection alone will almost certainly be lower than that of the surgical procedure. If many patients in the injection group need additional injections, medications, or surgery, however, the carbon footprint of a treatment strategy involving initial injections might be higher than that of a surgery-focused approach.

Having access to both clinical and carbon-footprint data for the same patient group is important for making sustainable treatment recommendations. If clinical outcomes are similar among study groups but carbon footprints differ, regulators and policymakers may recommend the low-carbon option. For example, the two anesthetic gases sevoflurane and desflurane have in many RCTs shown similar effectiveness in terms of the most important clinical end points.[2] However, 1 kg of sevoflurane has a global warming potential equal to the emission of 130 kg of carbon dioxide, whereas the same amount of desflurane has a global warming potential equal to 2540 kg of carbon dioxide (partly because it has a much longer atmospheric lifetime than sevoflurane).[3] Desflurane is nonetheless one of the most-used anesthetics in many countries. If carbon-footprint assessment had been included as an end point in clinical trials of anesthetic gases, desflurane might not have been cleared for marketing or widely implemented.

LCAs are increasingly being conducted for health care products and procedures.[4] Such assessments have been separate from trials measuring patient outcomes, however. If carbon footprint were defined as a secondary end point in clinical trials, these data would be included in trial publications and shared with a broader audience. Trialists could incorporate environmental impact analyses in studies, and regulators and editors could request that information on such analyses be included in funding applications, research protocols, and scientific papers.

Including environmental end points in RCTs could help clinicians, regulators, and policymakers understand the environmental effects of medical interventions by promoting awareness of the resource consumption and waste generation associated with health care services. Reporting carbon footprint alongside traditional efficacy and safety measures could also help ensure that decarbonization strategies are prioritized.

Learning health systems are emerging as a valuable approach for comparing interventions. These entities continuously gather and analyze data in real time, which creates a cycle of continuous learning and improvement within the health care system. This method has been used in pragmatic randomized trials and cancer screening programs.[5] Learning health systems could use environmental end points to enable faster, evidence-based implementation of low-carbon solutions in clinical practice.

We recognize that there are challenges associated with this proposal. Differences among health systems, including variation in energy sources and equipment, can mean that carbon-footprint analyses may not be generalizable across health care systems, countries, and regions. However, transparent LCAs permit identification of areas for improvement and include sensitivity analyses reflecting best- and worst-case scenarios. Identifying products, services, or procedures with high carbon costs may also

lead to opportunities for reducing carbon footprints in other areas of health care where similar interventions are used.

Another challenge involves the current lack of freely accessible databases containing information from LCAs of health care products and processes. As experience with requirements for clinical trial registries has made clear, transparency is crucial for facilitating reliable analyses and trustworthiness of results. To avoid "greenwashing" of health care services, pharmaceuticals, and other products, a predefined plan for environmental end-point analyses should be included in clinical trial registry databases and should specify LCA methods and be freely available. This framework might also encourage and facilitate the establishment of publicly available databases of health care LCA information.

Finally, integration of LCA methods into health care is in its early stages, and assessing environmental effects will require researchers to acquire new competencies. Although the International Organization for Standardization has published standards for conduct and reporting of LCAs that have been implemented in other industries, explicit standards for performing LCAs in health care are lacking. Despite these hurdles, the landscape of LCA in health care is evolving rapidly, with continuous improvements in databases and resources.[4] The tools needed to assess the carbon footprints of health care interventions are currently available. By integrating environmental impact analyses into RCTs, trialists could contribute to their refinement and use.

RCTs are the gold standard for evaluating the benefits and harms of medical interventions; their results have the potential to change clinical practice. Amid the climate crisis, we believe RCTs should address environmental impacts in addition to clinical effectiveness. Clinical trialists can support the use of evidence-based, sustainable approaches in clinical practice, thereby providing benefits for current and future patients.

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